EMS treated animals showed 1 white midventral spot. In the moxnidazole group, this could be observed in only 1 animal. All together 17 offspring with midventral white spots were found in the EMS group (additionally 1 with a midventral white-gray spot), 4 in the moxnidazole group and only 1 in the control animals. Main positions for colour spots for the EMS/moxnidazole group were in percent: head 0/20; back and sides 85/40; ventral 15/40. The low spontaneous frequency, the position and distribution of the spots are in good agreement with published data[2,6].

The results presented show that moxnidazole induces not only point mutations in microbes and *Drosophila* but also genetic alterations in mammalian somatic cells in vivo. Since mutagens of different types of action including a 5-nitroimidazole have proved to be active in the mammalian spot test, it can be expected that this test system will become a suitable procedure for routine testing of environmental mutagens and possibly carcinogens.

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Amnesic effects of intravenous diazepam and lorazepam

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Summary. The amnesic effects of 2 benzodiazepine drugs, diazepam (Valium) and lorazepam (Ativan), have been investigated. Some of the effects were similar to those of certain clinical amnesic syndromes. The effects were more extensive than previous work has indicated.

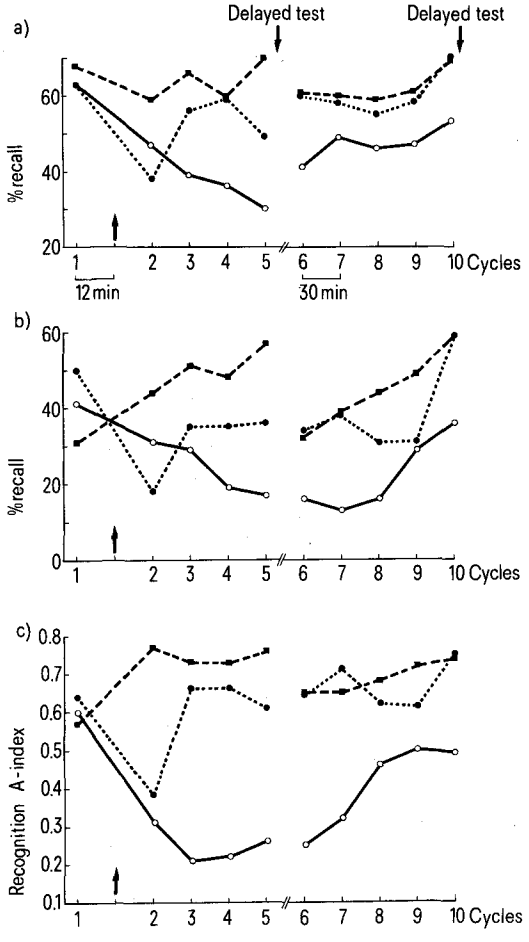
Amnesic effects have been reported[5–8] following i.v. injection of the benzodiazepines, diazepam (Valium) and lorazepam (Ativan). The effects of lorazepam have previously been investigated in a clinical setting under preoperative conditions, so that extensive testing of the subjects has not been possible. The present experiment was designed to show whether the amnesic effects of these 2 drugs are similar to those of certain clinical amnesic syndromes[9–11]. If they are, a more effective analysis of the syndromes becomes possible, since the onset and duration of the amnesia is then under experimental control and the same subjects can be tested with and without the drug. In addition, the drugs may be of value in analysing the neural basis of memory using experimental animals.

Material and methods. 2 cycles of memory tests (described below) were used to divide 27 medical student volunteers into 3 equal matched groups. 3 days later, on the day of injection, there were 10 further cycles. After cycle 1, either 2 ml of solution containing 7.5 mg diazepam or 3.0 mg lorazepam, or 2 ml of normal saline was given by slow i.v. injection. A double-blind procedure was employed. A cycle comprised: a) A list of 10 words from a single category, such as flowers, projected on to a screen for 20 sec. At the same time the words were spoken from prerecorded tape. The list was followed by 6 random digits. The task was immediate, ordered recall of the digits followed by free recall of the words. Recall was written in a booklet. b) Word completion. The 1st 3 letters of 10 5-letter words were provided in the booklet. After an initial attempt to write down the solutions, these were projected (feedback) and a 2nd attempt was made on another page of the booklet. c) Picture recognition. 2 colour-slides of landscapes were presented for later recognition. Following cycles 1–5 and 6–10 the materials presented in the previous 5 cycles were retested (delayed tests). Free recall of the word lists was cued by presenting the category names, e.g. 'flowers'. The recall test was followed by a recognition test in which the words were mixed with an equal number of new words from the same categories. Each word was rated as new or old on a 4-category scale. From the rating data, the A-index[12,13] was calculated: if recognition were all-or-none, this index would be equivalent to the proportion of original items genuinely recognized. Recognition of the pictures was evaluated by a similar method. New booklets were used for the retest of word completions. Immediately after the delayed tests, simple reaction times to an auditory stimulus were measured. Cycles 1–5 were before lunch and at 12-min intervals, apart from a double interval between cycles 1 and 2 for the injection. Cycles 6–10 were at 30-min intervals and commenced 200 min after injection. Thus the effects of the drugs were studied over a 5.5-h period. The results for 2 lorazepam subjects and 1 diazepam subject who failed to complete the experiment were discarded.

Results and discussion. Our major findings for the injection day were as follows: 1. With the exception of 1 lorazepam subject, immediate recall of digits was good on all cycles, with over 90% of sequences wholly correct. 2. Substantial impairment was found in the free recall of words in both immediate postdigit recall (figure, a) and delayed recall (figure, b). For cycles 2–5 combined, the 2 drug groups were significantly worse than the saline group both in the immediate and in the delayed tests ($p < 0.001$, based on one-way analysis of variance). For cycles 6–10 combined, the impairments were significant only for the lorazepam group ($p < 0.001$). The peak effect with diazepam on cycle 2, about 12 min after injection, is consistent with the findings of previous studies[5,6,8]. 3. Delayed recall of cycle 1 (figure, b) was better by the drug groups, although only the superiority of the diazepam to the saline group was significant ($p < 0.05$). This finding can be attributed to lowered

retroactive interference by the drug groups as a result of reduced learning on cycles 2-5[14]. A highly important implication is that the poor recall for cycles 2-5 by the drug groups cannot be attributed just to inefficient retrieval of stored information, since inefficient retrieval should affect recall of information from cycle 1 as well 4. The pattern of results (figure, c) for the delayed recognition tests is broadly similar to those found for free-recall. However, the superiority of the drug groups for cycle 1 has almost vanished. This result accords with the hypothesis that the superiority in recall is due to reduced retroactive interference (such interference is known to affect recall rather than recognition[15]). 5. Lorazepam, but not diazepam, affected recognition more than recall (figures, b and c) leading to an abnormal relationship between the 2 measures. Thus percentage recall subtracted from percentage recognition (A-index $\times 100$) was -1.8 for the lorazepam group as compared with 24.1 for the saline group for cycles 2-5: the difference was significant ($p < 0.01$). For cycles 6-10 the corresponding difference was in the same direction but non-significant. 6. For delayed picture recognition the diazepam group were significantly worse ($p < 0.05$) than the control group only for cycle 2. Thus, picture recognition did not reveal the full extent of the amnesia produced by this drug. The lorazepam group were significantly worse ($p < 0.01$) than the control group both for cycles 1-5 and for cycles 6-10. 7. Memory for word completions was similar for the diazepam and saline groups, even for cycle 2, and there were no significant differences. The lorazepam group was impaired at word completion even before feedback, perhaps because of the intellectual demands of this task. In consequence, no satisfactory basis for comparing retention of word completions by this group with that of the control group was available. 8. The difference in mean reaction time between the groups was small (< 90 msec) and there were no abnormally long individual reaction times. This result in conjunction with the good immediate recall of digits suggests that the subjects in the drug groups were able to remain alert. 9. The groups were indistinguishable when they were tested on new cycles 4 days after injection, showing that the effects of the drugs were fully reversible.

Results 1, 2 and 7 for the diazepam group and results 1, 2 and 5 for the lorazepam group constitute specific similarities between the amnesic effects of the drugs and those of certain clinical amnesic syndromes[9,16-18]. The most striking of these similarities concerns the abnormal relationship between recall and recognition in the lorazepam group. The high level of both recall and recognition shown by this group for material presented in the pre-injection cycle implies that the abnormal relationship is not produced by factors operating at the time of retrieval from memory. A clinically important aspect of our findings is that the effects of both drugs are more extensive than previous research[4-8] has indicated.



a Free recall of word lists immediately after recall of digits. The mean percentage recall (ordinate) is plotted against cycle number (abscissa) for the 2 drug groups (diazepam ●·····●, lorazepam ○----○) and the saline control group (■---■). Each subject received an injection (↑) between cycle 1 and cycle 2. Lunch was taken following the delayed test after cycle 5. Cycle 6 began 200 min after the injection. *b* Free recall of word-lists in delayed tests (after cycle 5 for cycles 1-5 and after cycle 10 for cycles 6-10). Axes as in *a*. *c* Recognition of words in delayed tests. The A-index (ordinate) is plotted against the cycle (abscissa) on which the word-list was originally presented.

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